



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
-----------------	-------------	----------------------	---------------------	------------------

10/564,474

11/20/2006

Robert Olivieri

002441.00186

9877

27476

7590

08/17/2009

NOVARTIS VACCINES AND DIAGNOSTICS INC.

INTELLECTUAL PROPERTY- X100B

P.O. BOX 8097

Emeryville, CA 94662-8097

EXAMINER

TONGUE, LAKIA J

ART UNIT

PAPER NUMBER

1645

MAIL DATE

DELIVERY MODE

08/17/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/564,474	Applicant(s) OLIVIERI ET AL.	
	Examiner LAKIA J. TONGUE	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 June 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-23 is/are pending in the application.
- 4a) Of the above claim(s) 8 and 16-23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7 and 9-15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 13 January 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>1/13/06</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's response to the Restriction Requirement filed on June 1, 2009 without traverse of Group I, claims 1-7 and 9-15 is acknowledged. Claims 1-23 are pending. Claims 8 and 16-23 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions. Claims 1, 8-10 and 13 have been amended. Claims 1-7 and 9-15 are currently under examination.

Information Disclosure Statement

2 The information disclosure statement (IDS) submitted on August 15, 2008 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the examiner has considered the information disclosure statement.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Claims 1-7, 9-12, 14 and 15 are rejected under 35 U.S.C. 102(e) as being anticipated by Zollinger et al. (U.S. Patent 6,558,677 B2).

The rejected claims are drawn to a process for preparing bacterial OMV's, comprising a step of ultrafiltration prior to any ultracentrifugation or sterilization steps.

Zollinger et al. disclose a process for preparing vaccines which comprise outer membrane vesicles from *N. meningitidis*. Zollinger et al. disclose that the vaccine can be prepared by isolating native outer membrane vesicles from the organism or from the culture medium by methods known in the art. Zollinger et al. disclose filtering to sterilizing the solution, diluting the solution, adding an adjuvant and stabilizing the solution (column 9, lines 1-9). Moreover, Zollinger et al. disclose that ultracentrifugation steps can be eliminated by use of the batch-wise adsorption of nucleic acid onto a DEAE ion exchange matrix followed by filtration to remove the ion exchange matrix and then ultrafiltration using a membrane or microfiltration, such as Ultrafiltration cartridge. Zollinger et al. disclose that ultracentrifugation steps were used to separate the OMV (see column 8, lines 43-51). Zollinger et al. disclose the use of centrifugation in a continuous flow sharples centrifuge (see column 14, line 23). Zollinger et al. disclose that the OMV can be added to a pharmaceutically acceptable diluent, carrier or excipient (see column 3, lines 13-16). Zollinger et al. disclose that the present invention include the use of *Neisseria meningitidis* Group B (see column 3, lines 23-25). Zollinger et al. disclose that the outer membrane protein is subject to phase variation in expression wherein mutants with constitutive expression of this protein replace the rmp protein with a copy of the opc gene (see column 6, lines 37-42).

The process of Zollinger et al. is identical to the instantly claimed invention. Absent evidence to the contrary, the ultrafiltration steps necessarily results in

Art Unit: 1645

diafiltration; is necessarily a cross-flow or tangential flow and necessarily has a cut off of about 300kDa.

4. Claims 1-7 and 9-13 are rejected under 35 U.S.C. 102(e) as being anticipated by Granoff et al. (U.S. 2006/0029621).

The rejected claims are drawn to a process for preparing bacterial OMV's, comprising a step of ultrafiltration prior to any ultracentrifugation or sterilization steps.

Granoff et al. disclose a process of preparing outer membrane vesicles prepared from the outer membrane of a cultured strain of *Neisseria meningitidis*. Said outer membrane vesicles can be obtained from said strain grown in broth by separating the bacterial cells from the culture medium by, for example, filtration or low speed centrifugation, affinity separation or high-speed centrifugation (see paragraph 0085). Granoff et al. disclose the use of adjuvants to enhance the effectiveness of the composition (see paragraph 0091). Moreover, Granoff et al. disclose the use of outer membrane vesicle from *Neisseria meningitidis* serogroup B strain H44/76 (B:15:P1.7,16) (see paragraph 0013).

The process of Granoff et al. is identical to the instantly claimed invention. Absent evidence to the contrary, the ultrafiltration steps necessarily results in diafiltration; is necessarily a cross-flow or tangential flow and necessarily has a cut off of about 300kDa.

Art Unit: 1645

5. Claims 1-7 and 9-15 are rejected under 35 U.S.C. 102(e) as being anticipated by Berthet et al. (U.S. 2006/0204520 A1).

The rejected claims are drawn to a process for preparing bacterial OMV's, comprising a step of ultrafiltration prior to any ultracentrifugation or sterilization steps.

Berthet et al. disclose a process for preparing bacterial OMV's by which vesicles from modified strains are reduced in size by sterile filtration (see paragraph 0058).

Preferably, the gram negative bacterium is *Neisseria meningitidis*, which has been genetically modified by down regulating expression of either or both of *exbB* and *exbD* genes (see paragraph 0056). Berthet et al. further disclose that one or more genes are preferred for down regulation they include *PorA*, *PorB*, *PilC*, *ThpA*, *TbpB*, *LbpA*, *LbpB*, *Opa*, and *Opc* (see paragraph 0092). Moreover, Berthet et al. disclose the effect of the *rmpM* mutation on OMV's from H44/76 (see paragraphs 0125-26). Berthet et al. disclose that the blebs may be filter sterilized and that the blebs can be harvested without the use of detergents, which would mean that usual process steps to remove detergent such as chromatography purification and ultra centrifugation may be obviated (see paragraphs 0036-37).

The process of Berthet et al. is identical to the instantly claimed invention. Absent evidence to the contrary, the ultrafiltration steps necessarily results in diafiltration; is necessarily a cross-flow or tangential flow and necessarily has a cut off of about 300kDa.

Art Unit: 1645

6. Claims 1-4, 6 and 9-12 are rejected under 35 U.S.C. 102(e) as being anticipated by Lowell et al. (U.S. Patent 6,476,201 B1).

The rejected claims are drawn to a process for preparing bacterial OMV's, comprising a step of ultrafiltration prior to any ultracentrifugation or sterilization steps.

Lowell et al. disclose a method of preparing meningococcal outer membrane protein proteosome preparations from *N. meningitidis* (see column 3, lines 14-17).

Lowell et al. disclose that the proteosome are prepared from group B meningococcal using hollow fiber diafiltration technology. Moreover, Lowell et al. disclose that other conventional ultrafiltration/diafiltration methods are envisioned (see column 3, lines 47-49 and 52-55). Lowell et al. disclose that the method has three stages, the last of which is sterile filtration (see column 4, lines 56-59). Lowell et al. disclose that the product is administered as a saline solution and adsorbed to aluminum hydroxide gel as an adjuvant (see column 8, lines 7-9).

The process of Lowell et al. is identical to the instantly claimed invention. Absent evidence to the contrary, the ultrafiltration is necessarily a cross-flow or tangential flow.

Conclusion

7. No claim is allowed.

Art Unit: 1645

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAKIA J. TONGUE whose telephone number is (571)272-2921. The examiner can normally be reached on Monday-Friday 8-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LJT
8/12/09

/Robert B Mondesi/

Supervisory Patent Examiner, Art Unit 1645